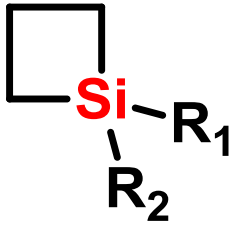
Annulation Reaction of Silacyclobutanes（SCBs）



Reporter：Zhan Shi

Supervisor：Prof. Ping Lu

Fudan University

2022.5.20

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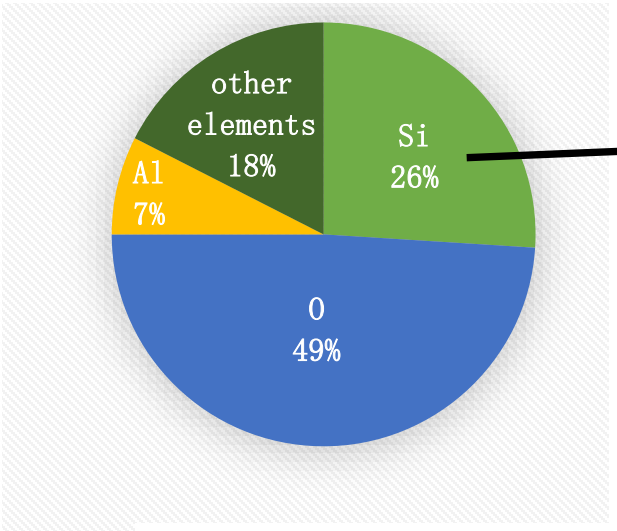
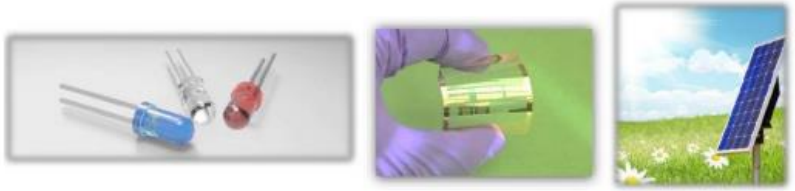




Achiral aryl silicon material

$Si^{\delta+}$ - $H^{\delta-}$ 

$C^{\delta-}$ - $H^{\delta+}$

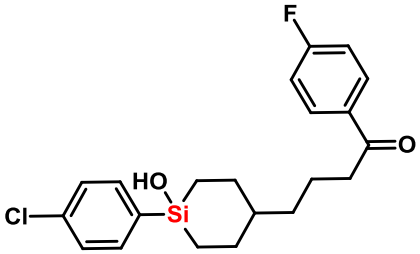
Atomic radium:	**117 pm**	**77 pm**
Electronegativity:	**1.90**	**2.55**

C → Si

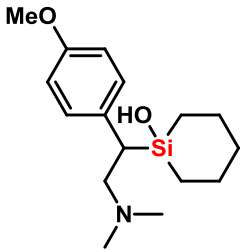
carbon-silicon switching

silicon incorporation

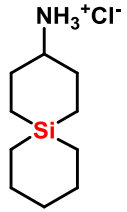
Bioactive Molecules



sila-*haloperidol*
(antipsychotic)

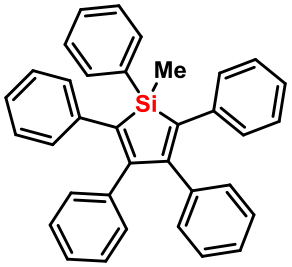


sila-*venlafaxine*
(antidepressant)

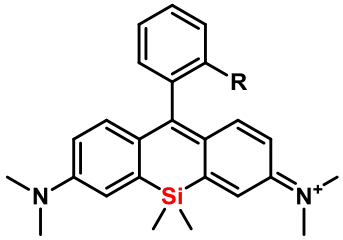


sila-*spirocyclic amines*
(influenza A virus inhibitor)

Materials Molecules

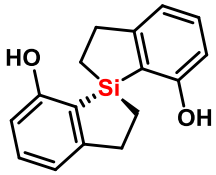


silole-*AIEgens*
(aggregation-induced
emission luminogens)



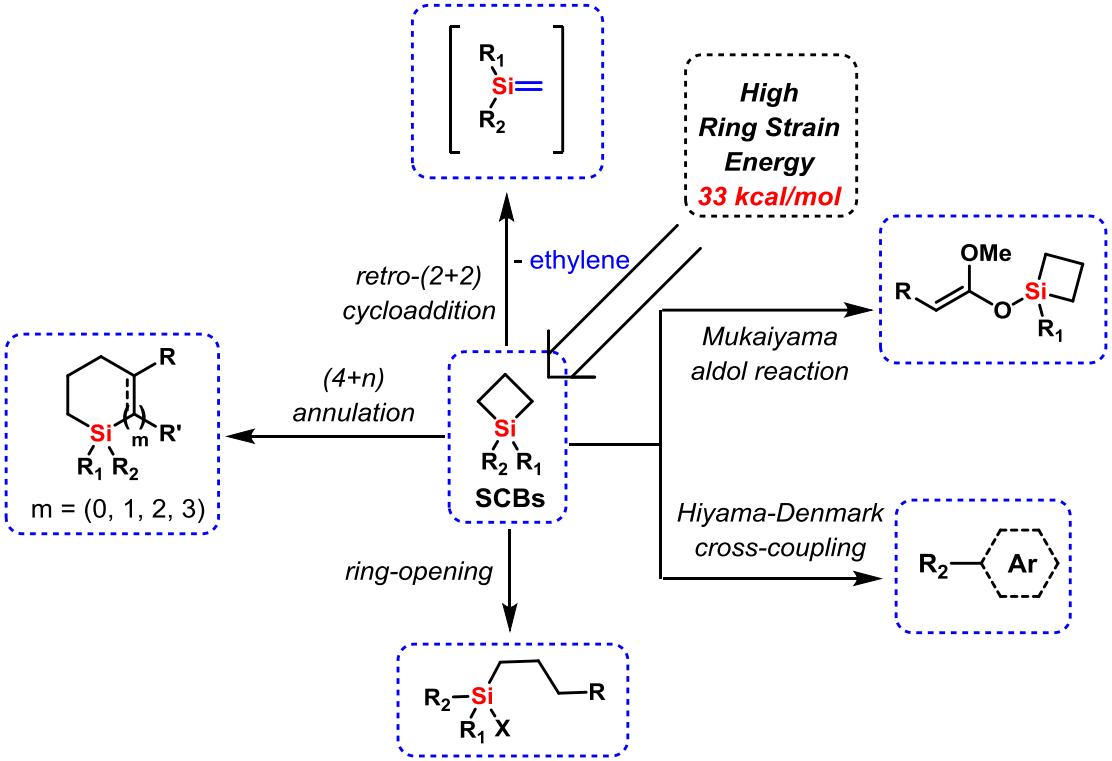
silole-*rhodamine*
(fluorescent probes)

Chiral Ligand Scaffolds



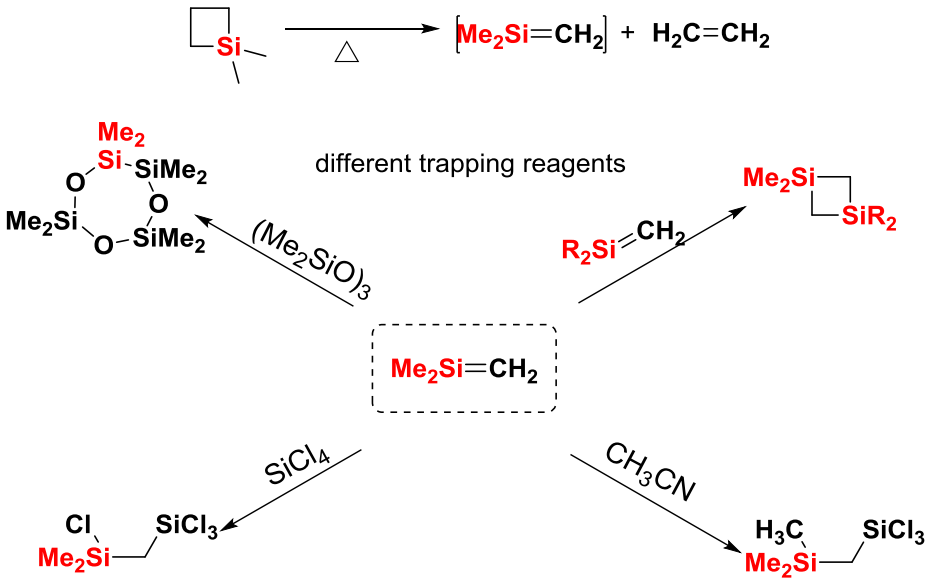
SPSIOL

Transformations of SCBs



Transformations of SCBs

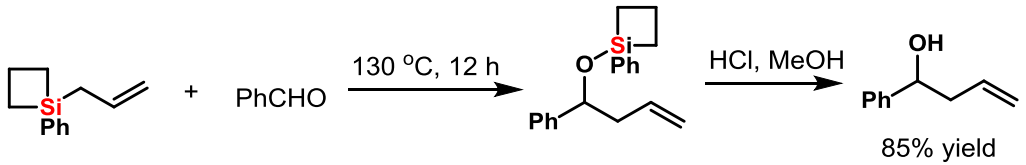
1. retro-(2+2) cycloaddition



Bush, R. D.; *J. Am. Chem. Soc*. **1975**, *97*, 7371.

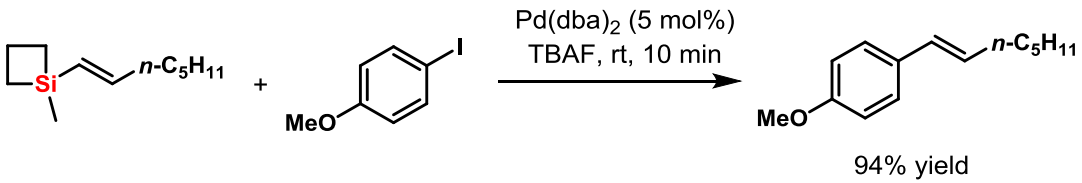
Transformations of SCBs

2. Mukaiyama aldol reaction



Utimoto, K..*J. Org. Chem.* **1994**, *59*, 7152.

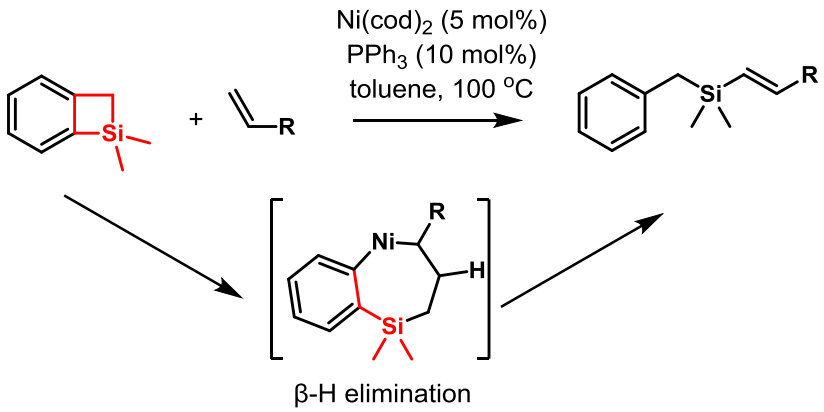
3. Hiyama-Denmark cross-coupling reaction



Denmark, S. E. *J. Am. Chem. Soc.* **1999**, *121*, 5821.

Transformations of SCBs

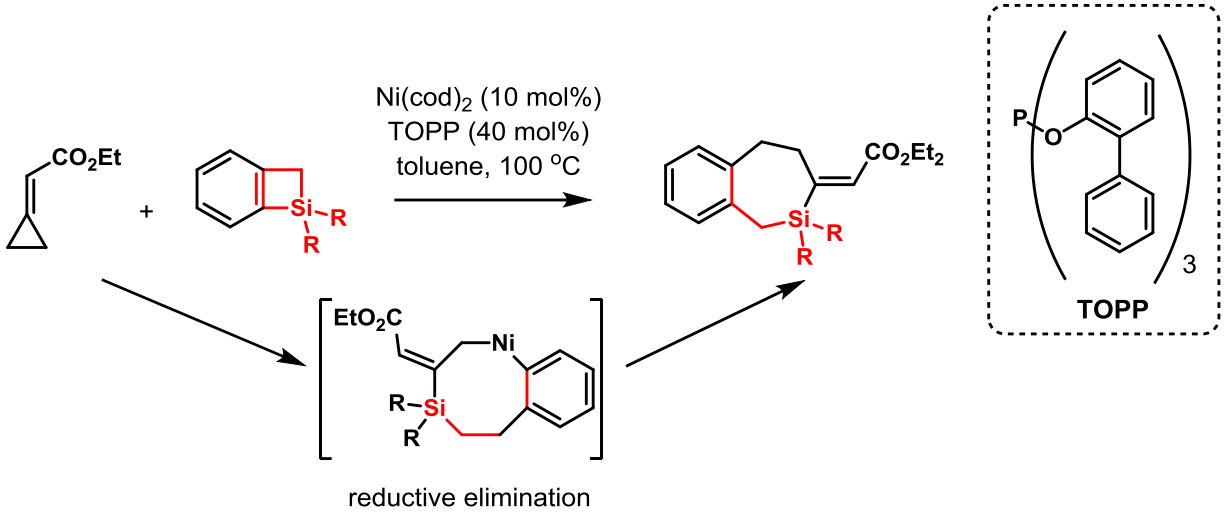
4. Ring-opening reaction



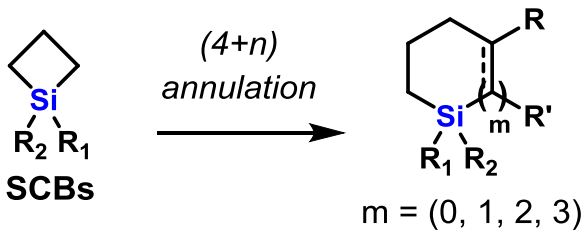
K. Oshima, *J. Am. Chem. Soc.*, **2007**, *129*, 6094.

Transformations of SCBs

5. Annulation reaction



Saito., *Tetrahedron Lett.*, **2010**, *51*, 6028.



challenges to controlling selectivity

- **regioselectivity**
- **chemo-:** ring opening *vs* ring expansion
- **configurational:** *Z- vs E-* alkene
- **enantio-:** Si* center

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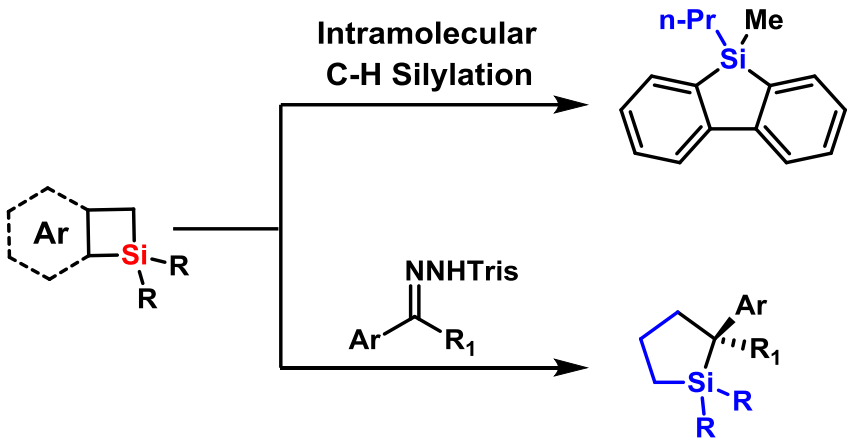
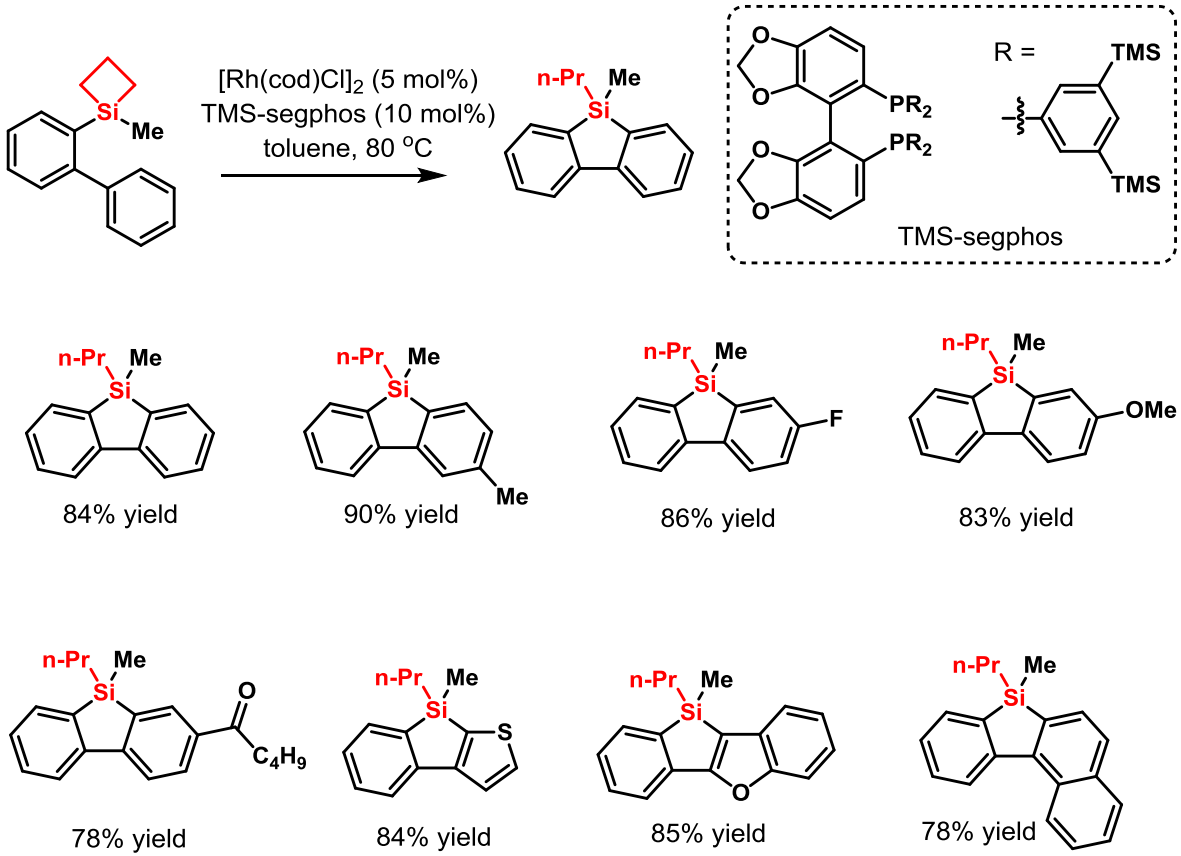
(4 + 1) Annulation Reactions



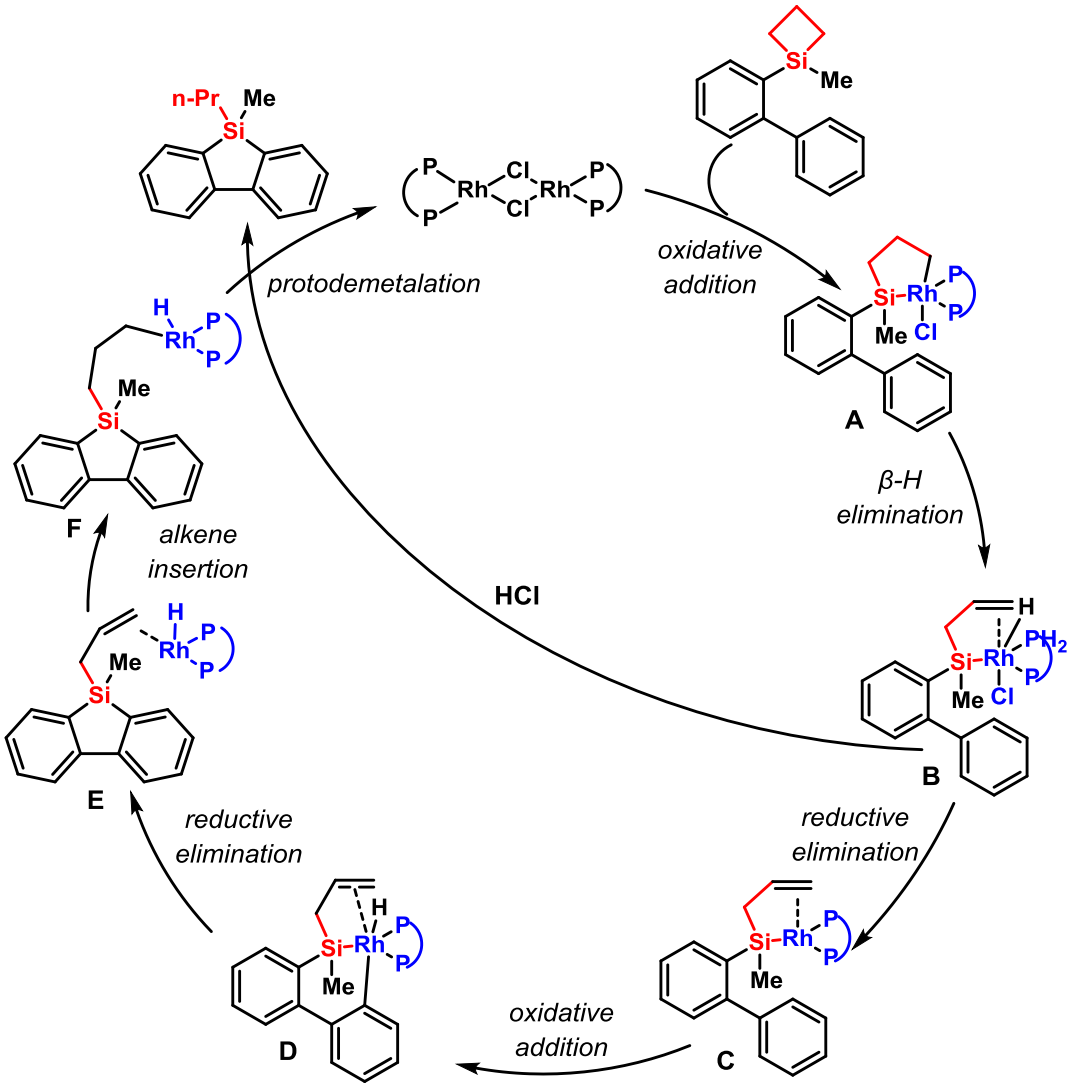
(4 + 1) Annulation Reactions through C-H silylation



He, W., *Angew. Chem., Int. Ed.*, **2016**, *55*, 6319.

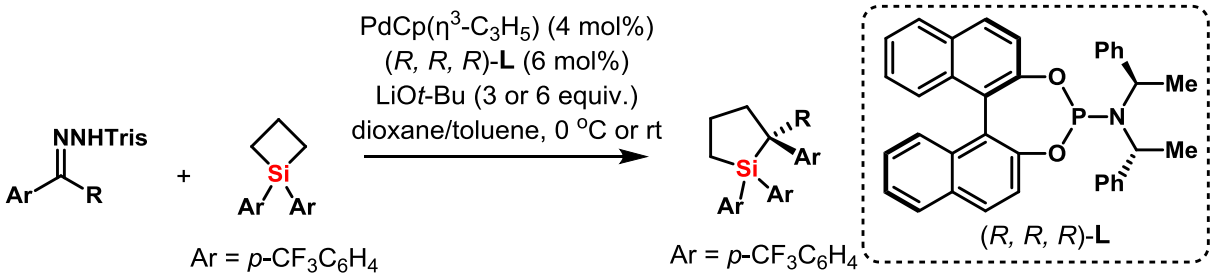
(4 + 1) Annulation Reactions through C-H silication

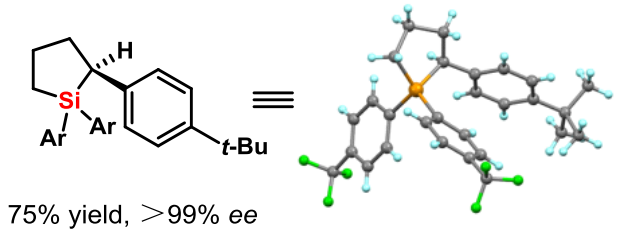
Mechanism



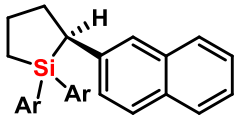
He, W., *Angew. Chem., Int. Ed.*, **2016**, *55*, 6319.

(4 + 1) Annulation Reactions with Carbene

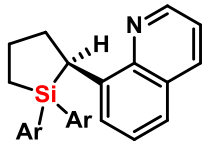




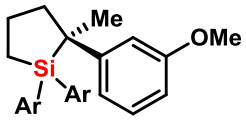
75% yield, ＞99% *ee*



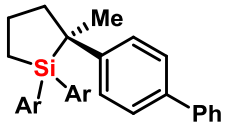
88% yield, ＞99% *ee*



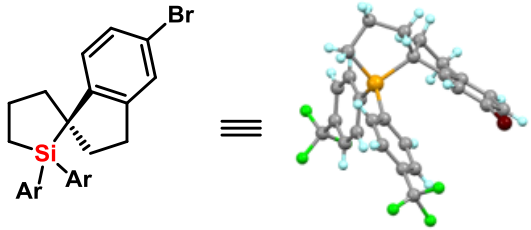
65% yield, 97% *ee*



78% yield, 91% *ee*



77% yield, ＞99% *ee*

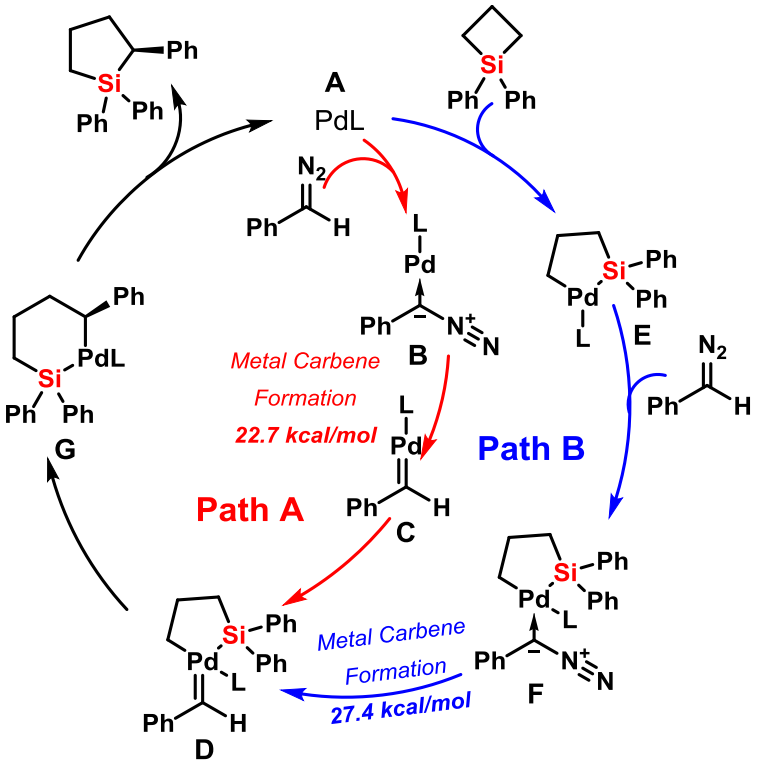


41% yield, 97% *ee*

Wang, J., B., *J. Am. Chem. Soc.* **2021**, *143*, 12968.

(4 + 1) Annulation Reactions with Carbene

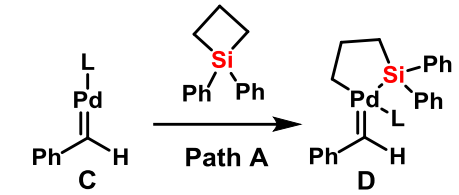
Mechanism



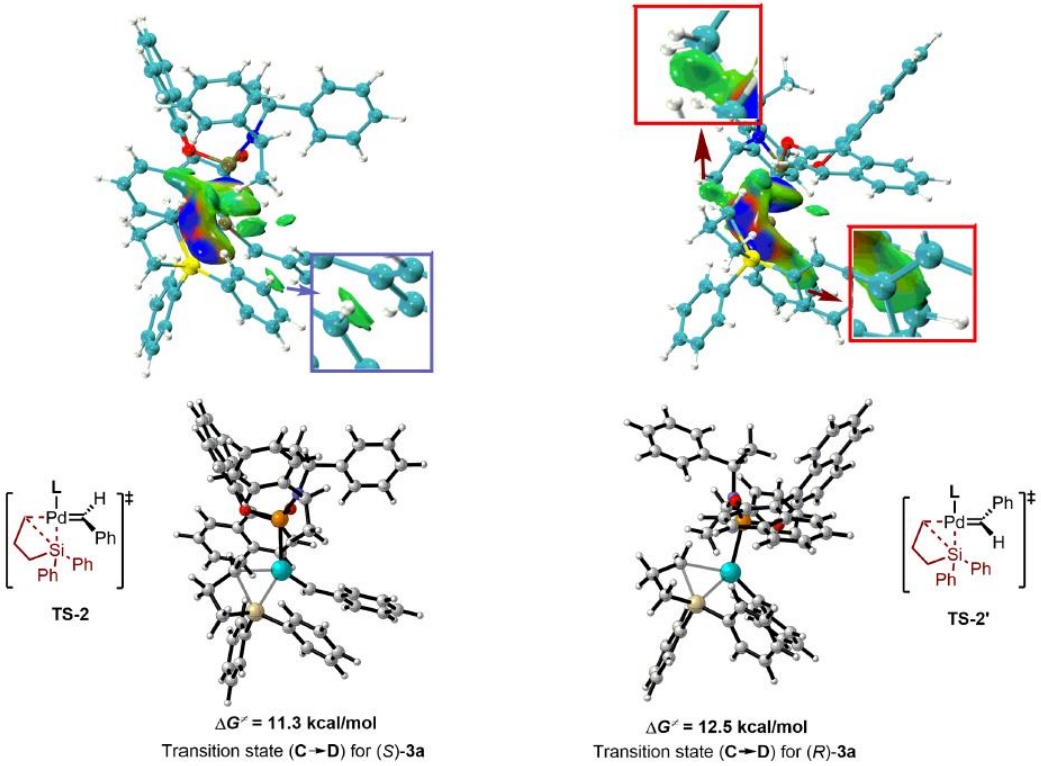
Wang, J., B., *J. Am. Chem. Soc.* **2021**, *143*, 12968.

(4 + 1) Annulation Reactions with Carbene

IGM analysis



enantioselectivity-determining step



Wang, J., B., *J. Am. Chem. Soc.* **2021**, *143*, 12968.

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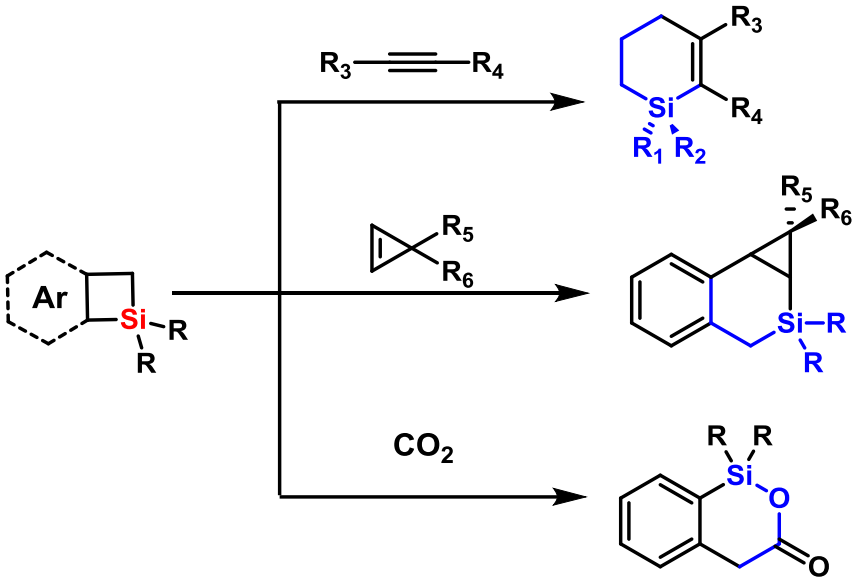
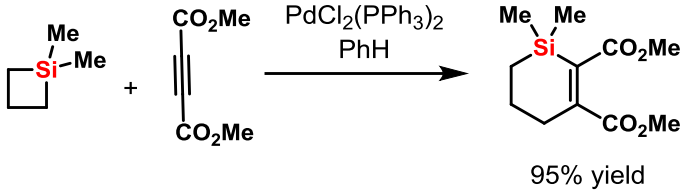
(4 + 2) Annulation Reactions



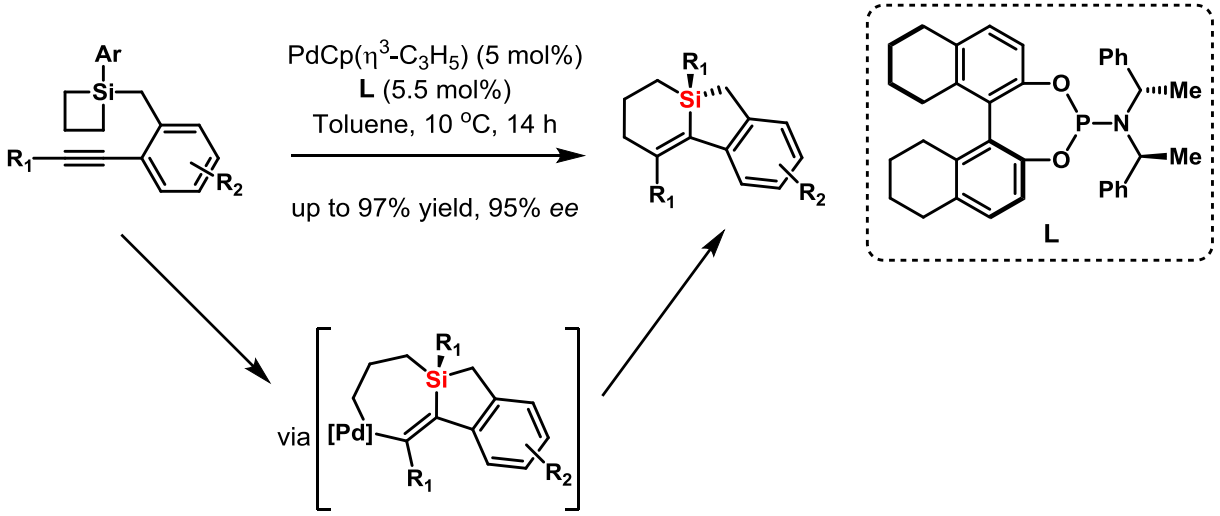
(4 + 2) Annulation Reactions with Alkynes

Intermolecular reaction



Sakurai, H., *Chem. Lett.* **1975**, *4*, 891.

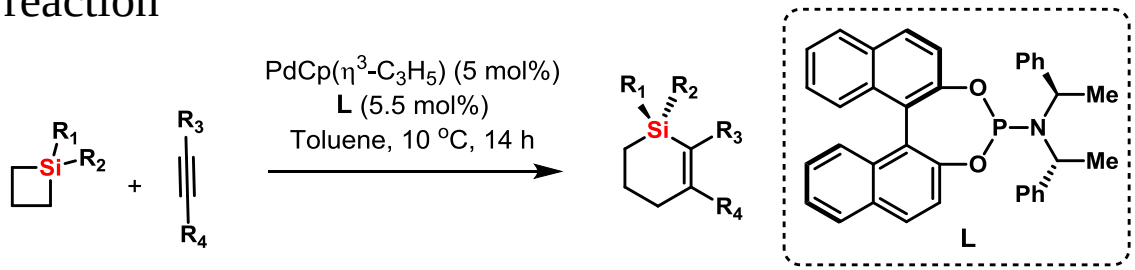
Intramolecular reaction

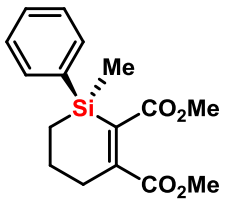


T. Hayashi, *J. Am. Chem. Soc.* **2011**, *133*, 16440.

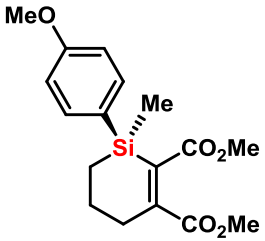
(4 + 2) Annulation Reactions with Alkynes

Intermolecular reaction

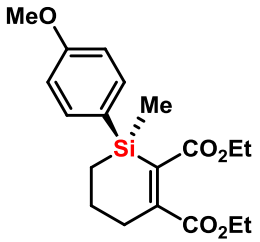




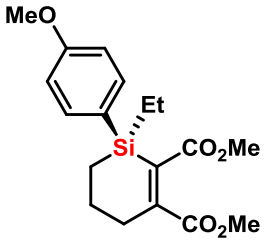
95% yield, 92% *ee*



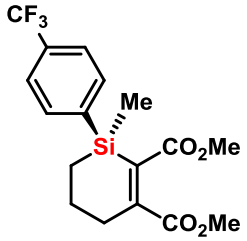
95% yield, 92% *ee*



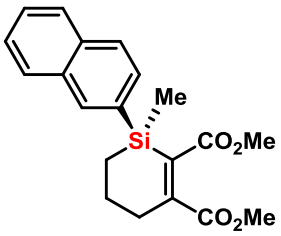
90% yield, 91% *ee*



90% yield, 91% *ee*



95% yield, 92% *ee*

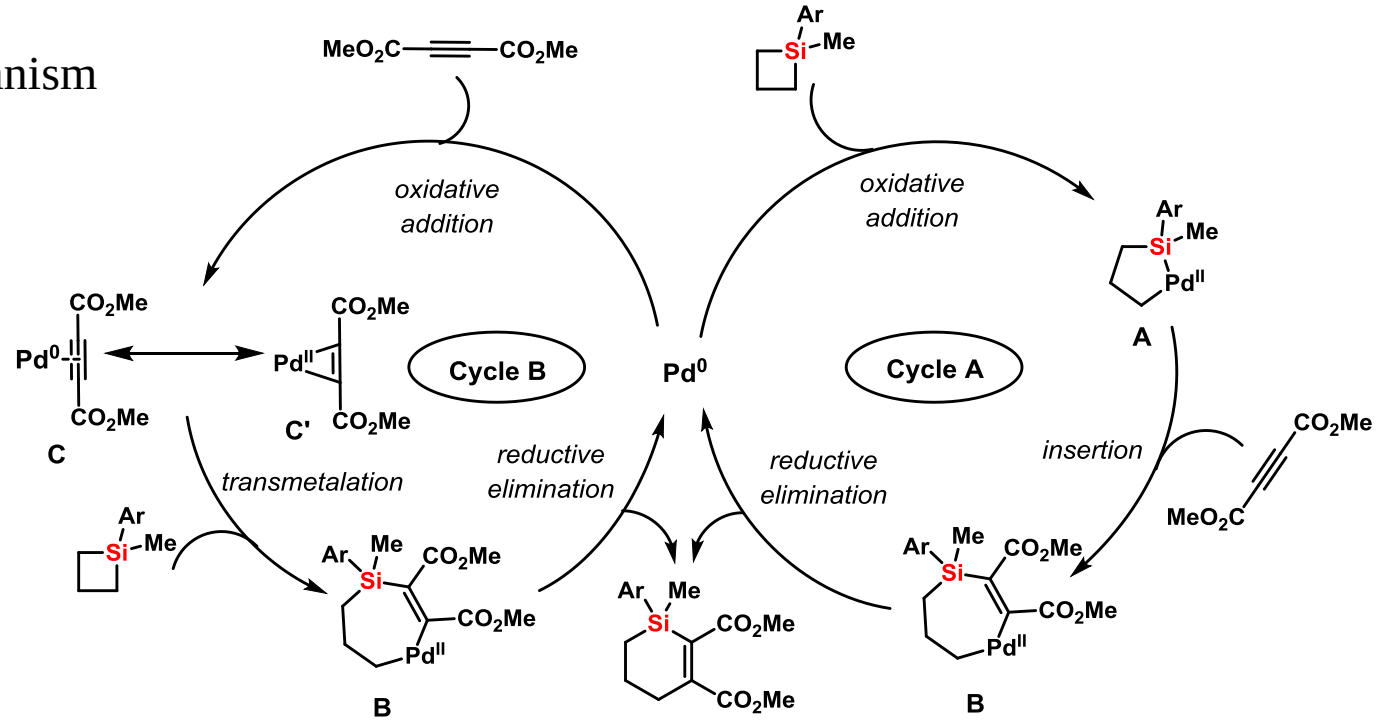


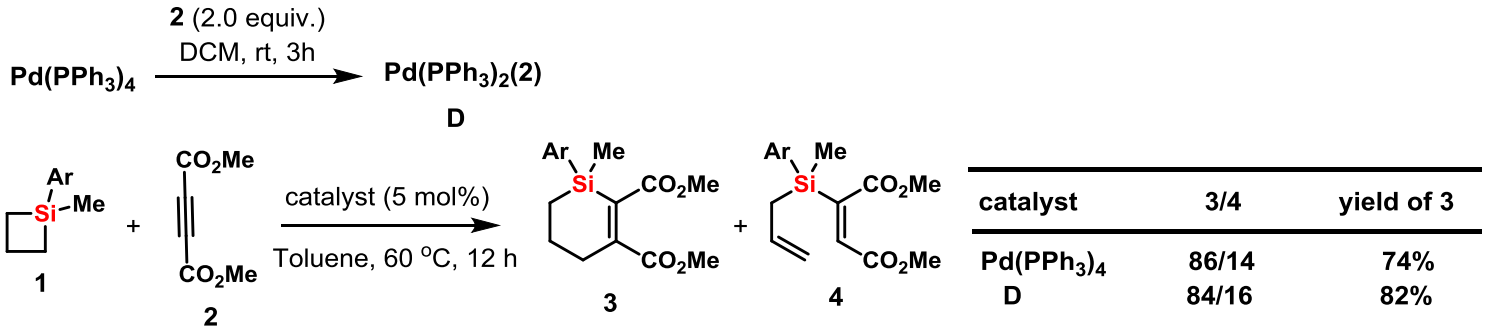
90% yield, 92% *ee*

T. Hayashi, *Org. Lett.* **2012**, *14*, 2902

(4 + 2) Annulation Reactions with Alkynes

Mechanism

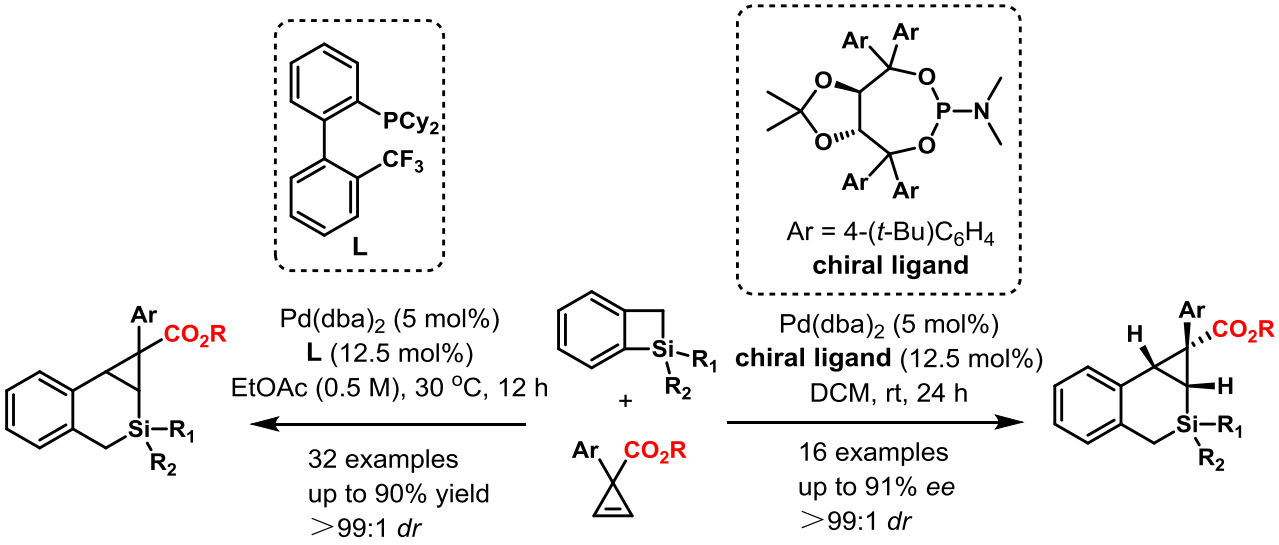




catalyst	3/4	yield of 3
$Pd(PPh_3)_4$	86/14	74%
D	84/16	82%

T. Hayashi, *Org. Lett.* **2012**, *14*, 2902

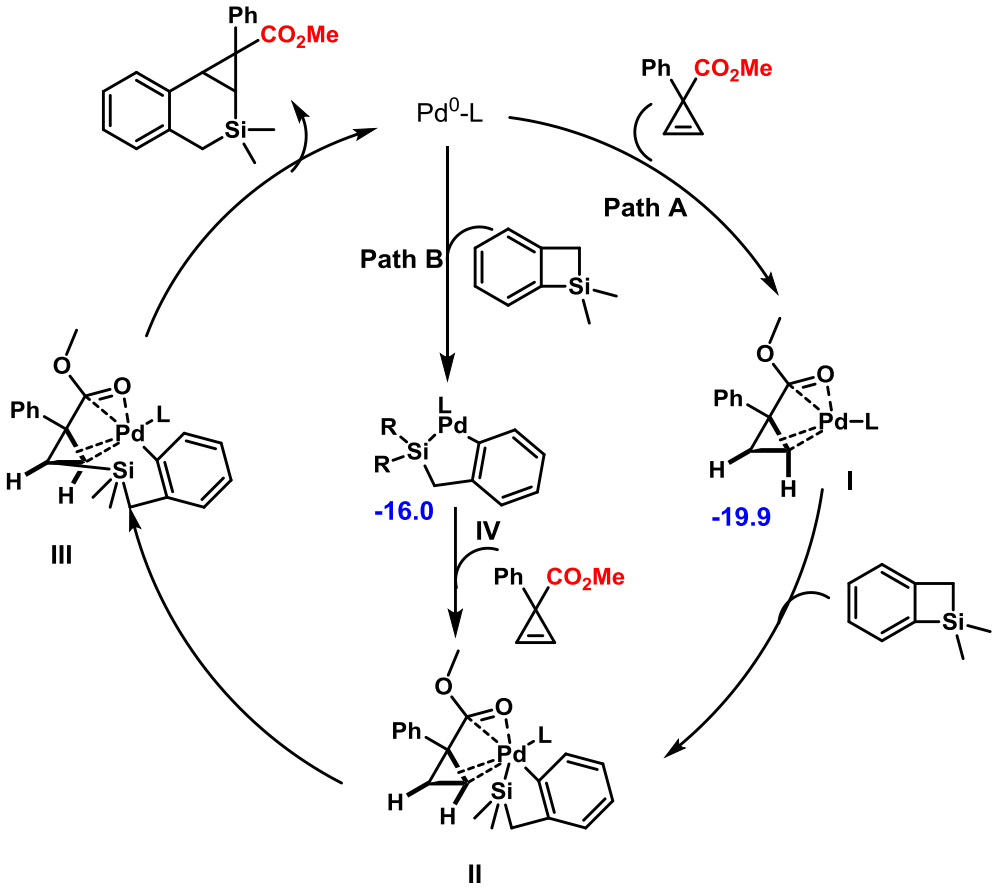
(4 + 2) Annulation Reactions with Cyclopropenes



Xu, L. W. *Angew. Chem., Int. Ed.* **2020**, *59*, 790.

(4 + 2) Annulation Reactions with Cyclopropenes

Mechanism

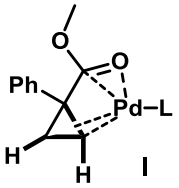


Xu, L. W. *Angew. Chem., Int. Ed.* **2020**, *59*, 790.

(4 + 2) Annulation Reactions with Cyclopropenes

^{31}P NMR Analysis

Prove the exist of



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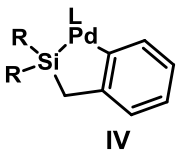
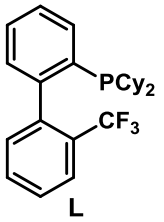
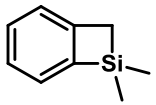


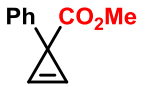
IV



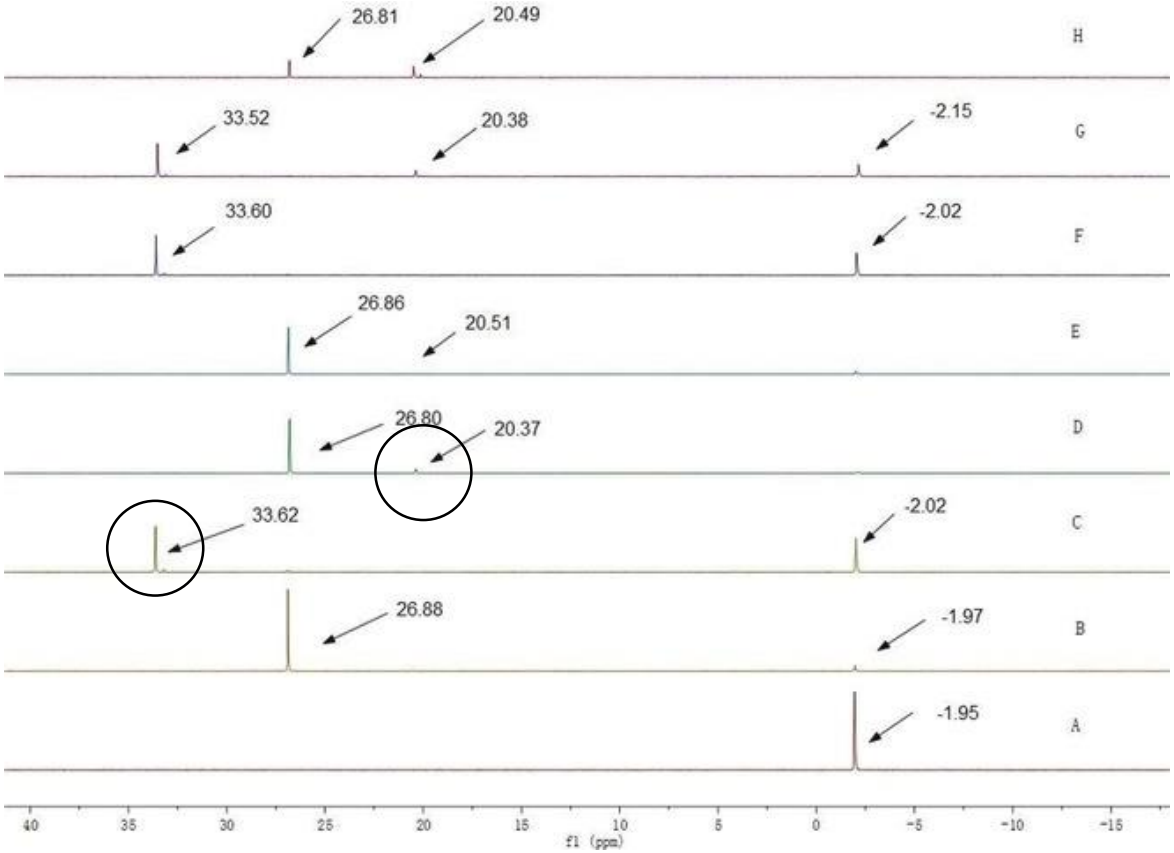
L



1a



2a



H) **L**, Pd(dba)$_2$, **1 a**, and **2 a** (2:1:50:10) the mixture was stirred for 12 h.

G) **L**, Pd(dba)$_2$, **1 a**, and **2 a** (2:1:50:10) the mixture was stirred for 15 min

F) **L**, Pd(dba)$_2$, **1 a**and **2 a** (2:1:10:10)

E) **L**, Pd(dba)$_2$, and **1 a** (2:1:10)

D) **L**, Pd(dba)$_2$, and **1 a** (2:1:50)

C) **L**, Pd(dba)$_2$, and **2 a** (2:1:10)

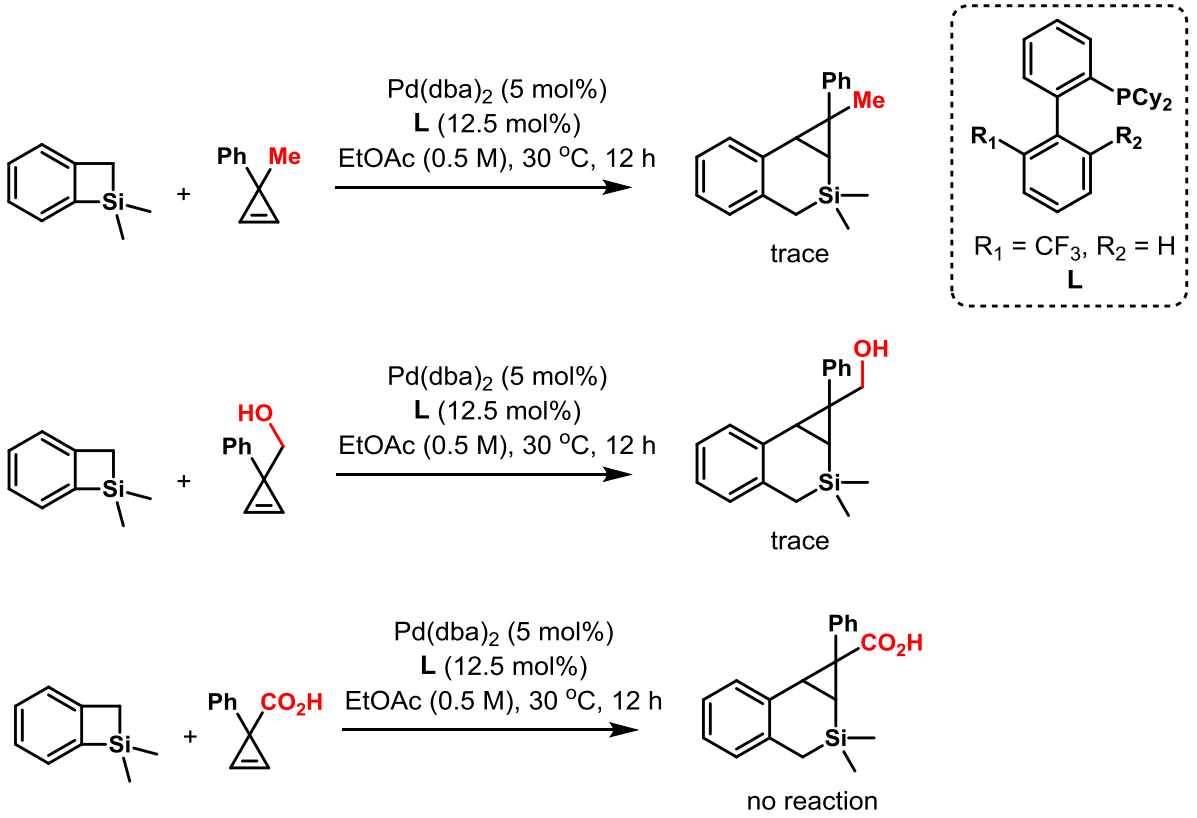
B) **L** and Pd(dba)$_2$ (2:1)

A) only **L**

Xu, L. W. *Angew. Chem., Int. Ed.* **2020**, *59*, 790.

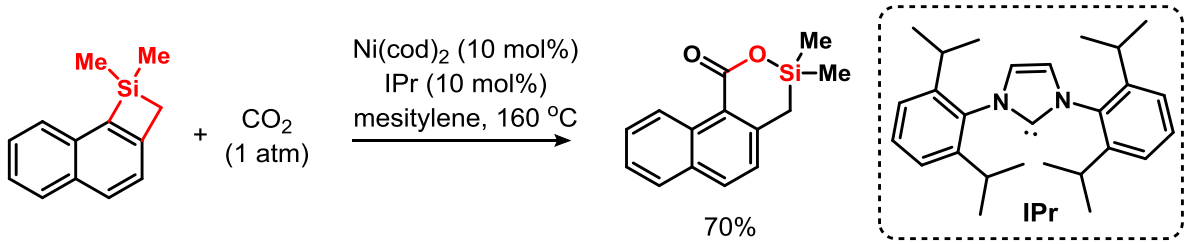
(4 + 2) Annulation Reactions with Cyclopropenes

The importance of the ester moiety on cyclopropenes

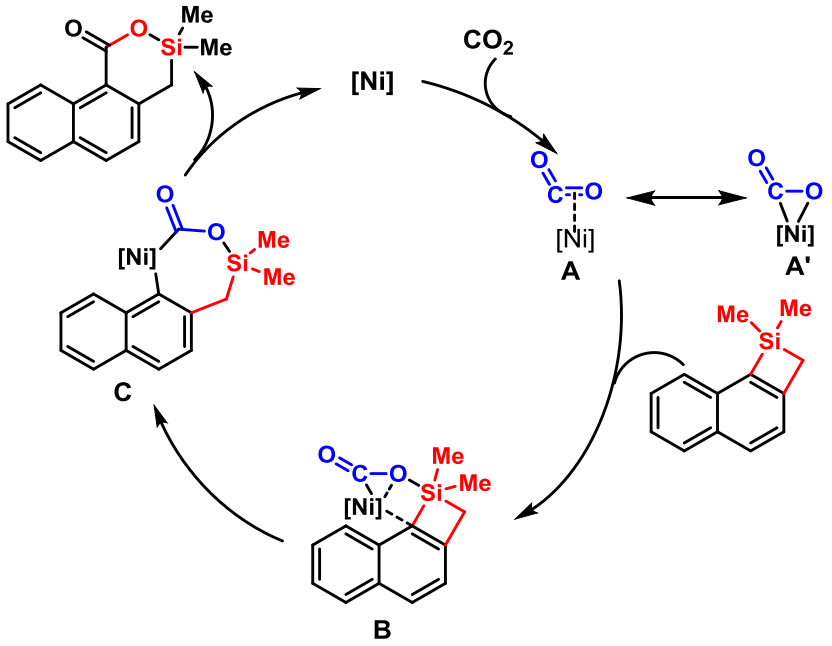


Xu, L. W. *Angew. Chem., Int. Ed.* **2020**, *59*, 790.

(4 + 2) Annulation Reactions with CO_2



Mechanism



M. Murakami, *Chem. Lett*. **2018**, *47*, 570.

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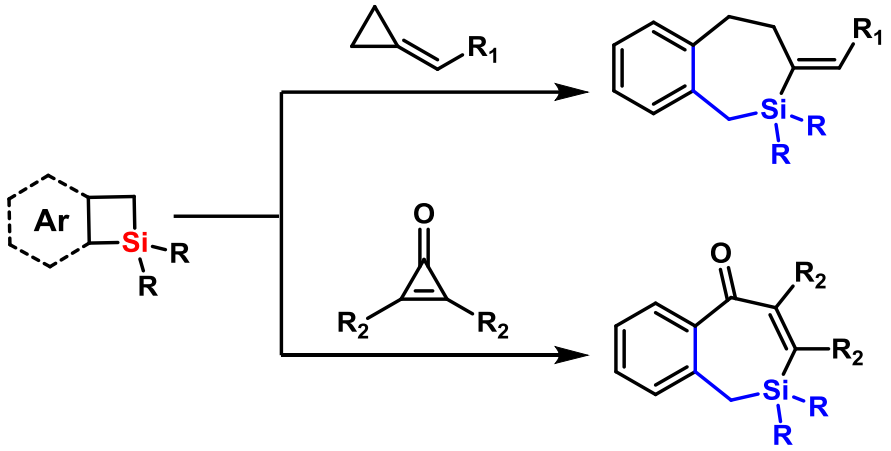
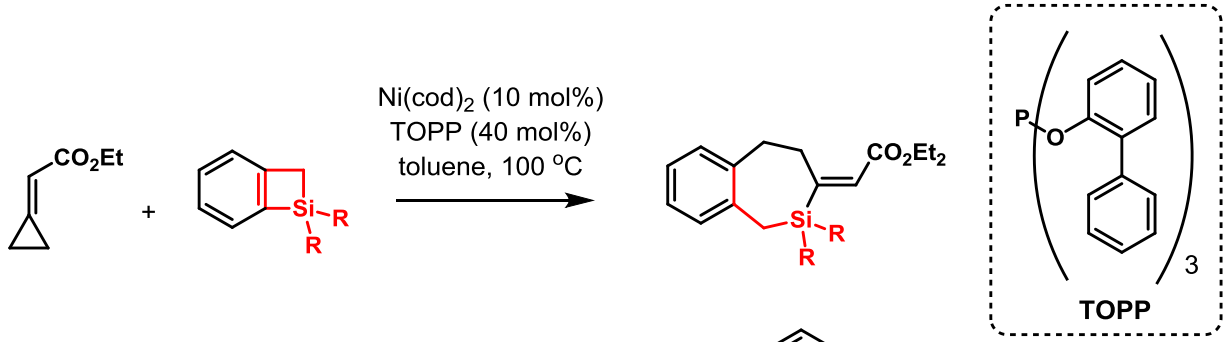
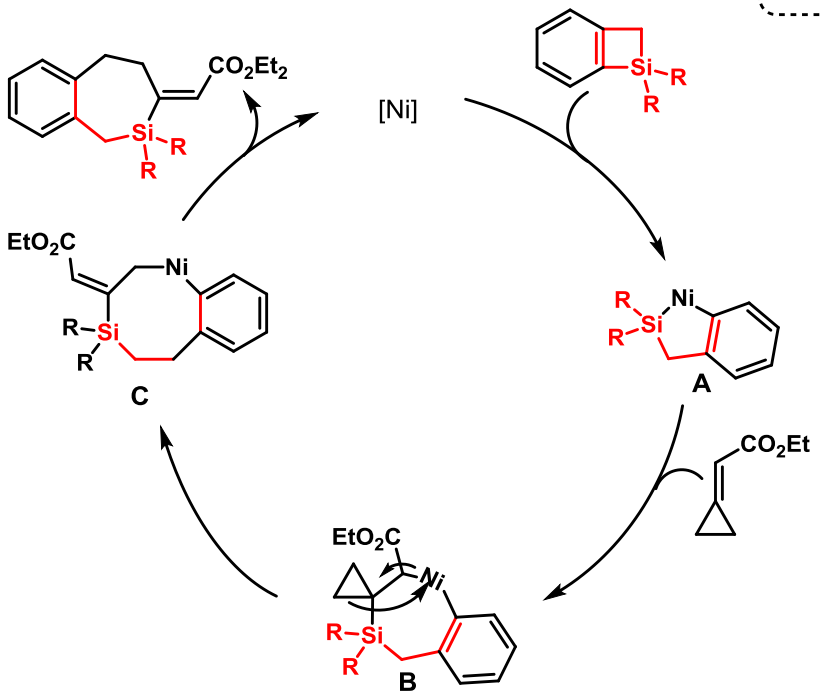
(4 + 3) Annulation Reactions



(4 + 3) Annulation Reactions with cyclopropylideneacetate

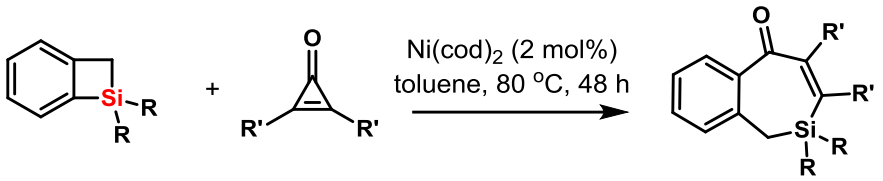


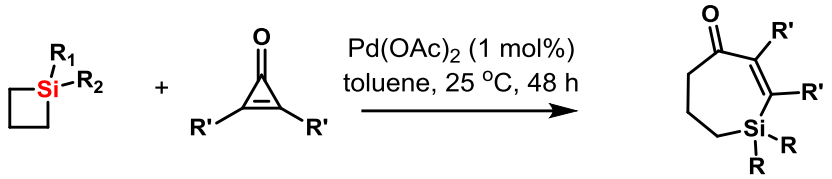
Mechanism



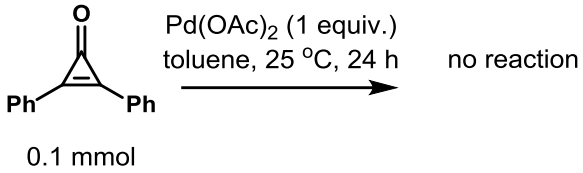
Saito., *Tetrahedron Lett*., **2010**, *51*, 6028.

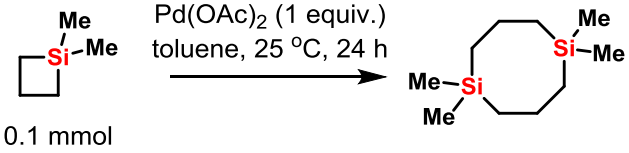
(4 + 3) Annulation Reactions with Cyclopropenones

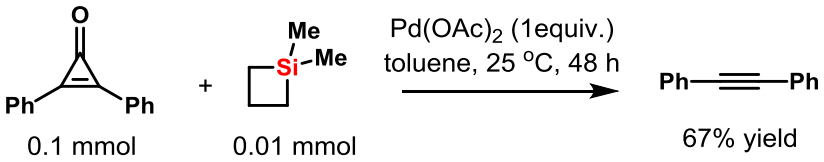




Mechanistically insightful experiments



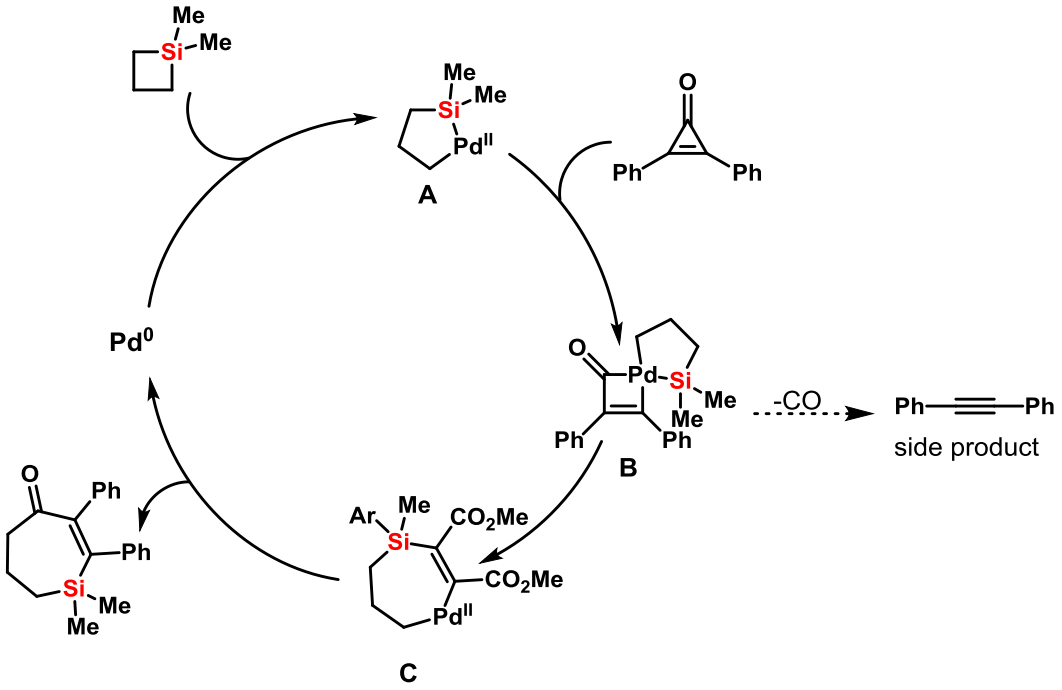




Zhao, D., *Angew. Chem., Int. Ed.*, **2018**, *57*, 6329.

(4 + 3) Annulation Reactions with Cyclopropenones

Mechanism



Zhao, D., *Angew. Chem., Int. Ed.*, **2018**, *57*, 6329.

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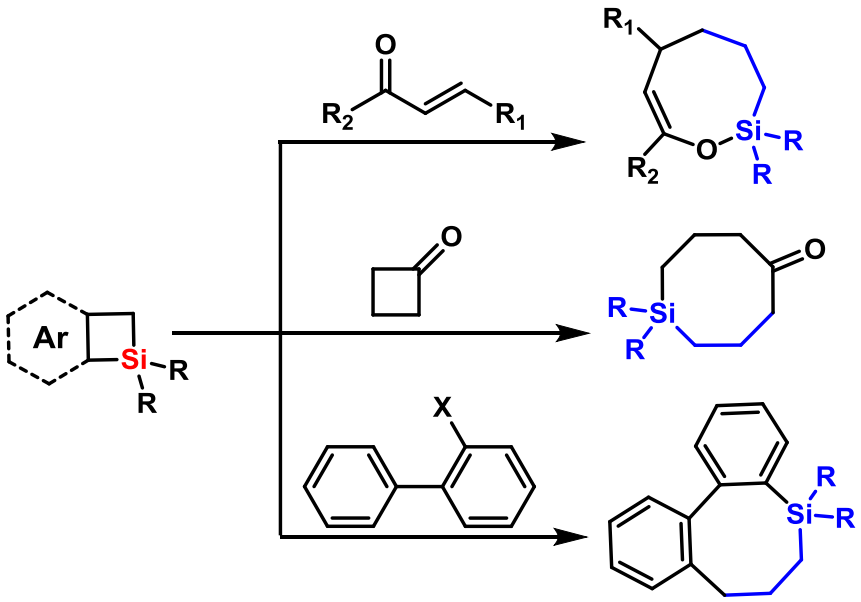
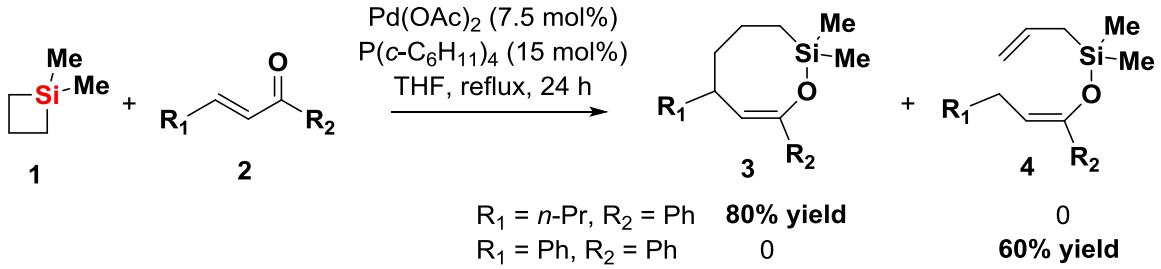
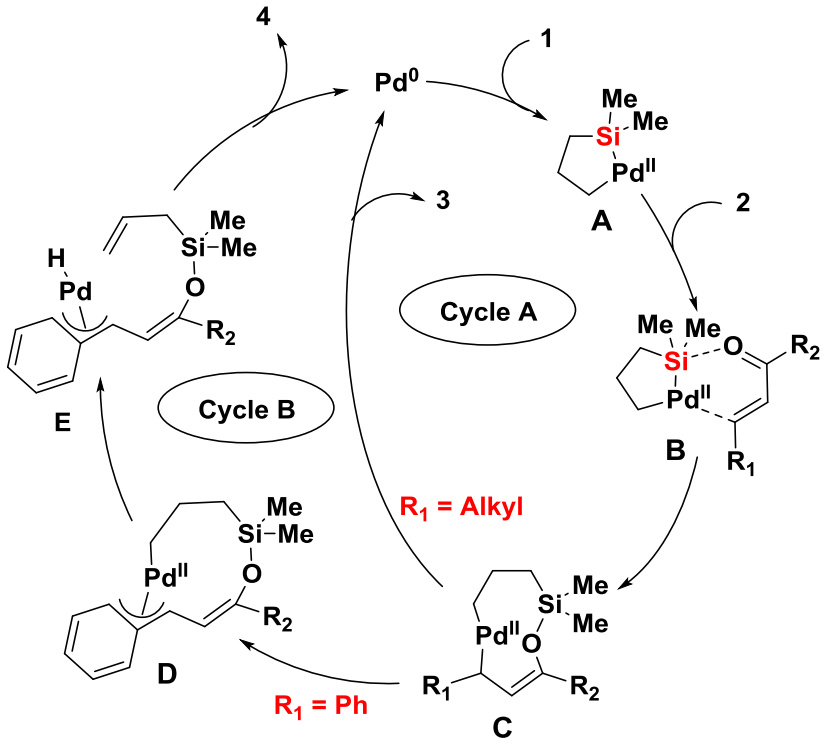
(4 + 4) Annulation Reactions



(4 + 4) Annulation Reactions with Enones



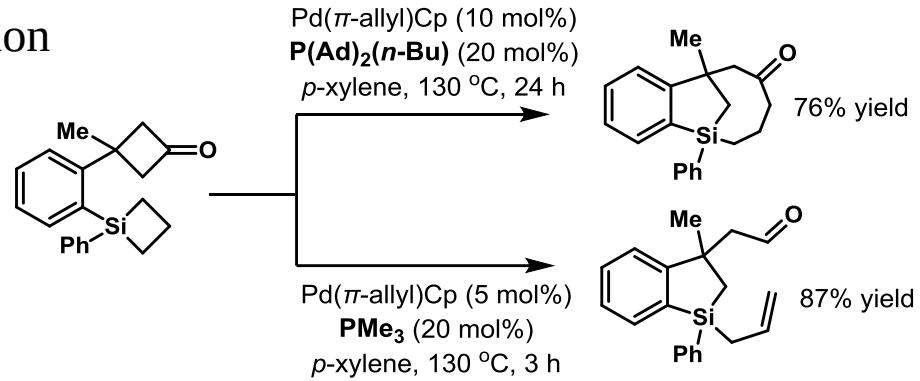
Mechanism



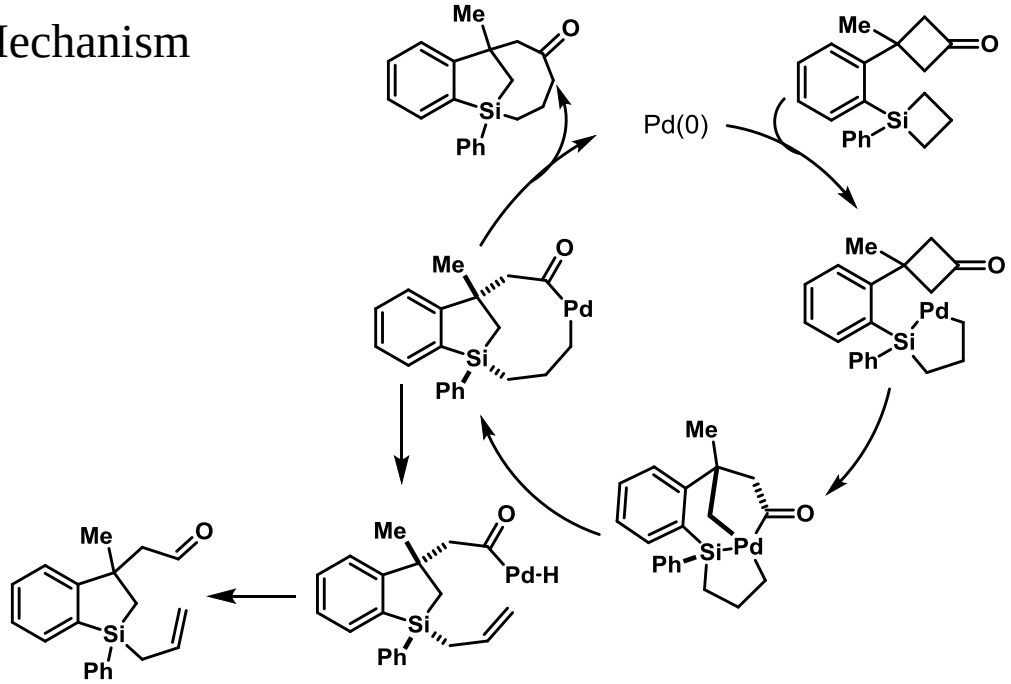
Oshima, K., *Org. Lett.*, **2008,** 10, 2199.

(4 + 4) Annulation Reactions with cyclobutanone

Intramolecular reaction



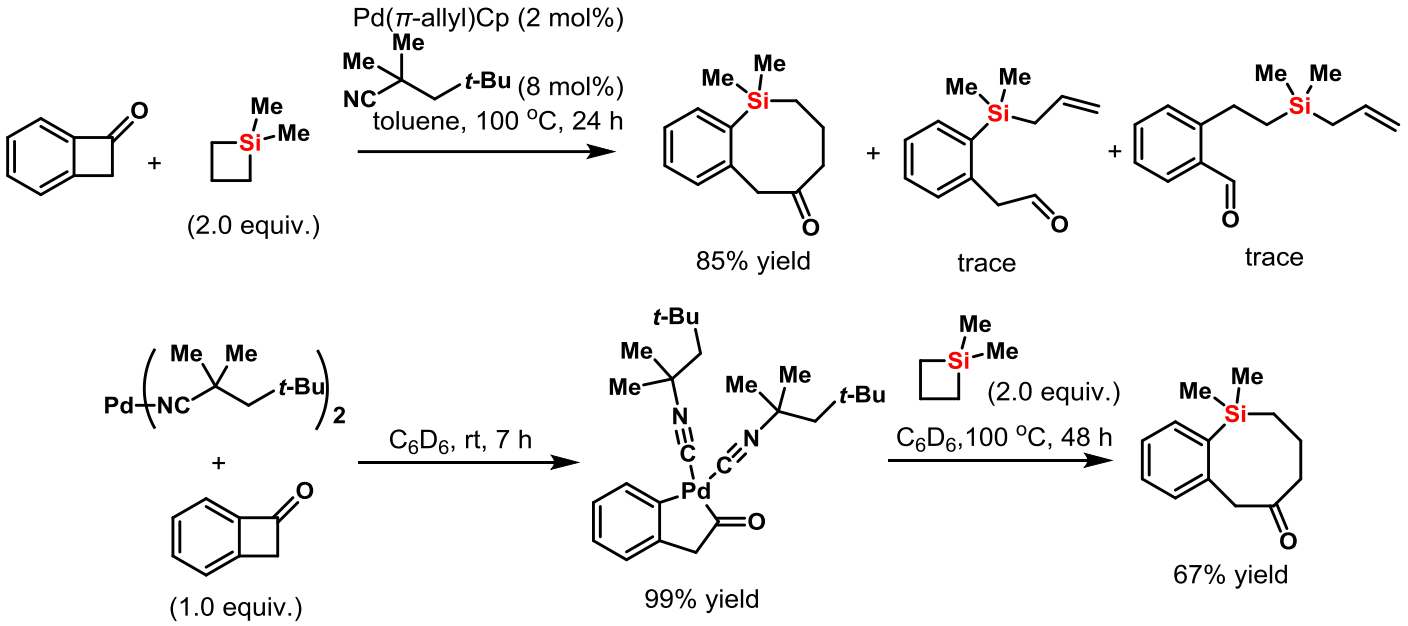
Mechanism



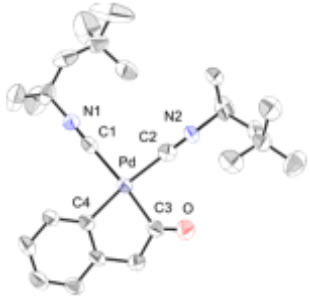
Murakami, M., *J. Am. Chem. Soc.* **2014**, *136*, 5912.

(4 + 4) Annulation Reactions with cyclobutanone

Intermolecular reaction

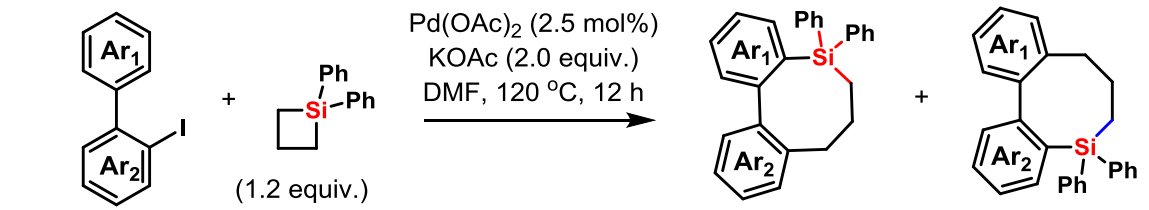


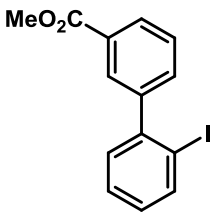
Intermediate



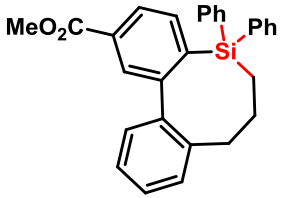
Murakami, M. *J. Am. Chem. Soc*. **2017**, *139*, 12414.

(4 + 4) Annulation Reactions with 2-Iodobiarenes

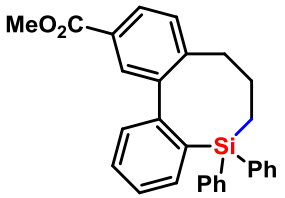




1a



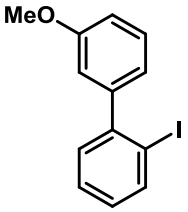
2a



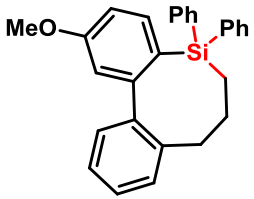
3a

2a:3a = 10:1

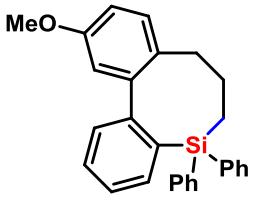
61%



1b



2b



3b

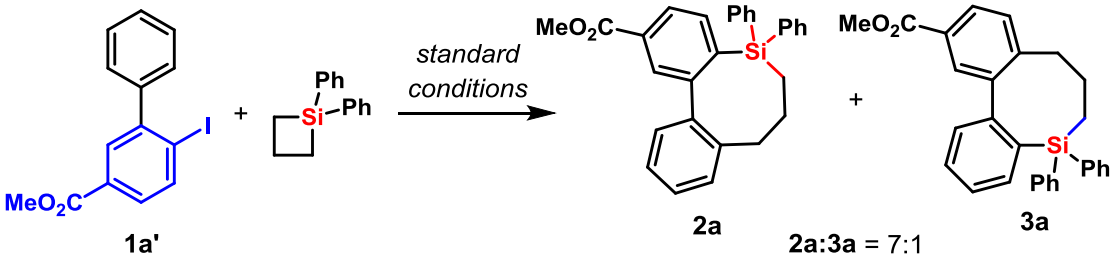
2b:3b = 1:5

61%

Liu, W., *ACS Catal*. **2021**, *11*, 5703.

(4 + 4) Annulation Reactions with 2-Iodobiarenes

i. Reaction with 1a'

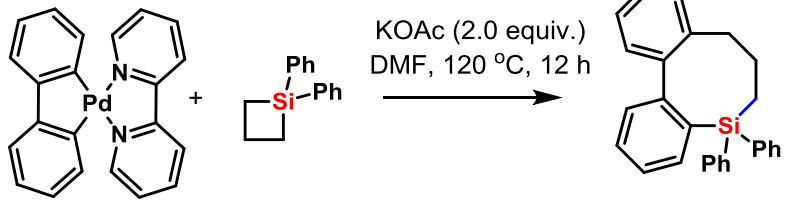


1a' + 2a + 3a

2a:3a = 7:1

63% yield

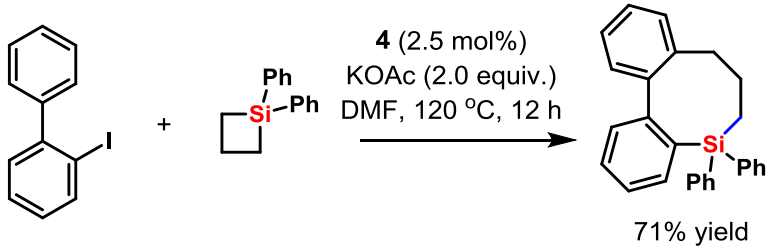
ii. Stoichiometric Expeiment



4

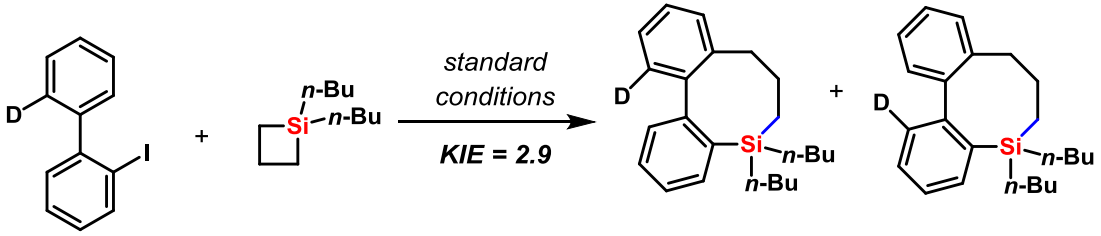
86% yield

iii. Catalytic Expeiment



71% yield

iv. Kinetic Isotope Effect

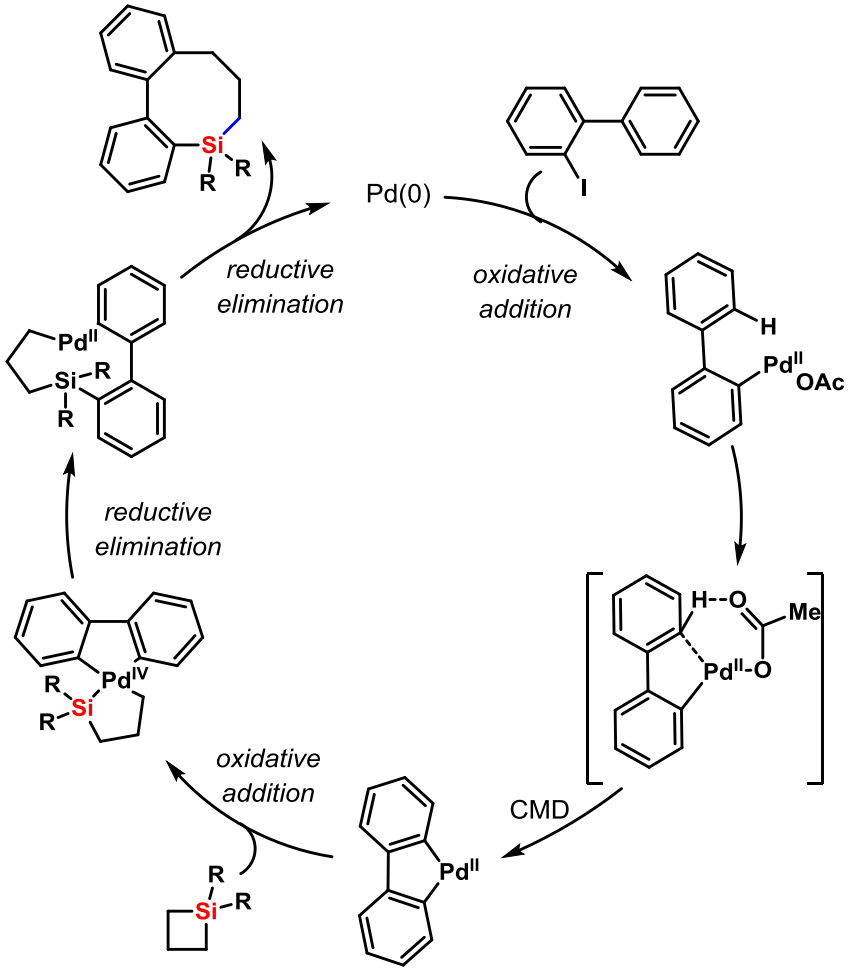


81% yield (75% D)

Liu, W. B., *ACS Catal*. **2021**, *11*, 5703.

(4 + 4) Annulation Reactions with 2-Iodobiarenes

Mechanism



Liu, W. B., *ACS Catal*. **2021**, *11*, 5703.

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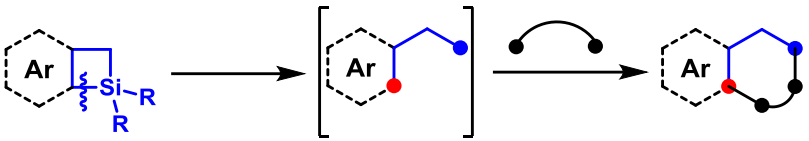
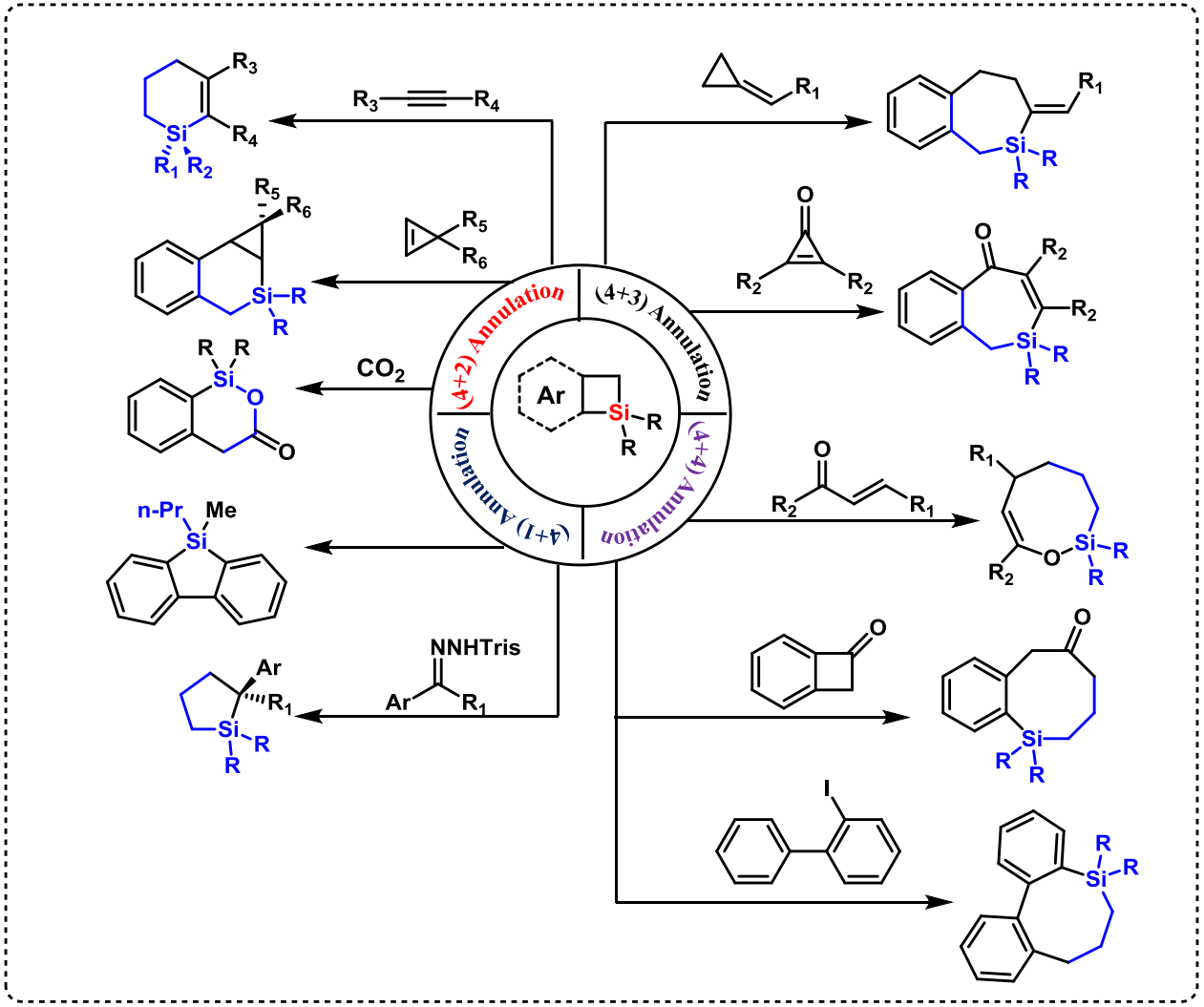
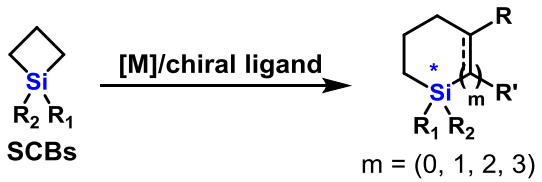
High Ring Strain Energy
33 kcal/mol

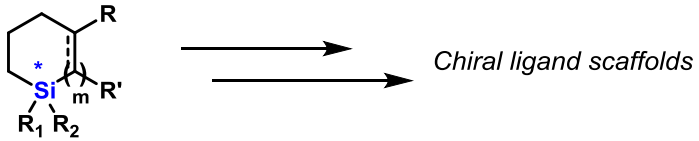




Construction more powerful catalytic systems



New ligand design



Synthesis of new material and bioactive molecules

Thanks for your attention!